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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/578,955	05/10/2006	Robert K. Evans	21575P	8652

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MERCK AND CO., INC
P O BOX 2000
RAHWAY, NJ 07065-0907

EXAMINER	
CHEN, STACY BROWN	
ART UNIT	PAPER NUMBER
1648	
MAIL DATE	DELIVERY MODE
07/14/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/578,955	EVANS ET AL.	
	Examiner	Art Unit	
	Stacy B. Chen	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 May 2009*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10 and 21-32* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10 and 21-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *10 May 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment and remarks filed March 19, 2009 and May 27, 2009 are acknowledged and entered. Claims 1-10 and 21-32 are pending and under examination. All objections/rejections over cancelled claims are moot.

Response to Amendment

2. The following objections/rejections are withdrawn:

- The objection to the specification is withdrawn in view of Applicant's amendment.
- The objection to claim 30 is withdrawn in view of Applicant's amendment.
- The rejection of claims 1, 9 and 31 under 35 U.S.C. 102(b) as being anticipated by Gao *et al.* (WO 01/40455 A2, "Gao") is withdrawn in view of Applicant's amendment. The claims now require a specific concentration of chlorobutanol (CB) that is not taught or fairly suggested in Gao.

Claims Summary

3. The claims are directed to a live adenovirus formulation comprising 0.25% to 0.6% (w/v), or 0.4% to 0.6% (w/v) chlorobutanol (CB) and various inhibitors of free radical oxidation, buffers, cryoprotectants, salts, divalent cations and non-ionic detergents. Also claimed is a vaccine vial comprising the formulation, and a method of preserving a live adenovirus formulation using CB.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, 9, 10, 21, 22 and 29-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gao *et al.* (WO 01/40455 A2, "Gao"). The claims are summarized above. Gao discloses live, recombinant adenovirus vectors for pharmaceutical use comprising a preservative, such as chlorobutanol (see page 19, first paragraph). The adenovirus concentration taught by Gao is in the range of 10^{10} to 10^{18} for an adult human having a weight of about 80 Kg (see page 19, fourth paragraph).

Gao fails to teach the specific range of CB concentration. However, it would have been well within the ability of the ordinary artisan to determine which concentration of CB would have been appropriate for preserving the live adenovirus vectors. Given Gao's suggestion to use CB, the ordinary artisan would have then performed routine tests to determine the concentration of CB that can preserve the live viruses without compromising the integrity of the viruses.

Gao does not specifically teach that the formulation of live adenovirus contains CB in the amount of a lowest effective concentration of CB up to the solubility limit of CB for the formulation. However, Gao teaches that CB is used as a preservative in a live, recombinant adenovirus composition for administration. It would have been obvious to one of ordinary skill in the art and well within the ability of that individual to use an amount of CB that is effective for the purpose of preservation without exceeding the solubility limit for the formulation.

Gao does not specifically teach the use of a multi-dose or single dose vial, however it would have been obvious to use a vial to store the contents of the formulation in order to contain and protect the formulation for delivery, storage and subsequent use. Gao discloses that the formulation of live, recombinant adenovirus can be administered using any suitable route, such

as intravenous, intramuscular, etc. (see page 19, second paragraph). If one were to administer Gao's composition using a needle, then the formulation would necessarily come from a vial of some sort. As for the multi-dose or single dose vial, it would have been obvious and well within the ability of the ordinary artisan to package the contents of the vials according to the desired use. Gao teaches that the dose may be repeated as desired (see page 19, fourth paragraph). Therefore, the claimed embodiments would have been obvious at the time the invention was made.

Applicant's arguments have been carefully considered but fail to persuade. Applicant's substantive arguments are primarily directed to the following:

- Applicant argues that Gao's suggestion to use commonly known preservatives was not followed by tests confirming their usefulness in any virus formulation. Applicant argues that it could not be reasonably predicted whether preservatives known to be useful in FDA approved drugs (suggested by Gao) would be useful as preservatives for viruses. Applicant points to their own experimentation with 10 commonly used preservatives, only two of which (CB and benzoic acid) were found to provide adenovirus stability.
  - In response to Applicant's argument, the Office first notes that the issue at hand is not whether it is obvious to use CB because Gao teaches the use of CB with a live, adenovirus composition. It appears that the issue Applicant is raising is whether Gao's teaching to use CB is enabled. Gao's suggestion to use CB is a constructive reduction to practice. Actual reductions to practice are not required as long as there is a reasonable expectation of success that CB will work as a preservative in a live, adenovirus composition. Lacking evidence to the contrary (*i.e.*, teachings that

dissuade one from ever using CB in live, adenovirus formulations) Gao's suggestion to use CB as a preservative is sufficiently enabled.

- Applicant argues that the combined teachings of the prior art cast doubt as to whether these preservatives (i.e., the preservatives listed in Gao's disclosure), including CB, would be useful with live adenovirus formulations. Applicant points to IDS Ref. C03 (Gray *et al.*, 1974), Tables III and IV, showing the destructive effect of CB on measles virus viability at a concentration of 0.5%. Applicant also points to Ref. C12 (Romanowski *et al.*, 1999), showing that a solution containing 1% CB caused a significant reduction in adenovirus titers after 14 days. Applicant asserts that based on these teachings, one would not reasonably expect CB to be an acceptable preservative for a live adenovirus composition.
  - In response to Applicant's arguments, the Office has considered the references of Gray *et al.*, and Romanowski *et al.* With regard to the Gray *et al.* reference, the teachings regarding CB and measles are noted, however, the relationship between CB and measles virus is not relevant to CB and adenovirus. (Note that Gao specifically suggests the use of CB with live, adenovirus formulations.) With regard to the Romanowski *et al.* reference, the concentration of CB used is higher than what is instantly claimed. It would have been well within the ability of the ordinary artisan to determine the appropriate concentration of CB to use in a given situation. After considering Romanowski's teachings, one would not have been dissuaded from ever using CB as a preservative in a live, adenovirus formulation. One of ordinary skill in the art would have considered the results in light of the differences in the content of

the compositions and the intended application of the compositions, and then would have made adjustments to the concentration of CB in relation to the amount of virus in the composition.

5. Claims 3-8 and 23-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gao *et al*. (WO 01/40455 A2, "Gao") as applied to claims 1 and 21 above, and further in view of Evans *et al*. (WO 01/66137 A1, "Evans"), for reasons of record. Applicant's arguments have been addressed above.

Conclusion

6. No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stacy B. Chen whose telephone number is 571-272-0896. The examiner can normally be reached on M-F (7:00-4:30). If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

/Stacy B Chen/
Primary Examiner, Art Unit 1648